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Zolmitriptan Nasal Spray

DEFINITION

Zolmitriptan Nasal Spray is an aqueous solution of zolmitriptan, supplied in a form suitable for nasal administration. It contains NLT 90.0% and NMT 110.0% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$).

IDENTIFICATION

Change to read:

- **A.**  **SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K**  (CN 1-MAY-2020)

Standard: Add 300 µL of a solution of 2.5 mg/mL of [USP Zolmitriptan RS](#) in [methylene chloride](#) to about 200 mg of dried [potassium bromide](#). Allow the mixture to dry. Grind the residue.

Sample: Add the contents of NLT 5 units of Nasal Spray to a container with 3 mL of 0.1 M [sodium hydroxide](#). Extract into a sufficient volume of [methylene chloride](#) to obtain a final concentration of about 1.0–2.5 mg/mL of zolmitriptan in the extract. Dry the extract over [anhydrous sodium sulfate](#). Add a suitable volume of the extract containing about 0.8 mg of zolmitriptan to about 200 mg of dried [potassium bromide](#). Allow the mixture to dry. Grind the residue.

Acceptance criteria: Meets the requirements

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Diluent: 0.02 M [hydrochloric acid](#)

Mobile phase: Acetonitrile and [water](#) (135:865). Add 1 mL of [trifluoroacetic acid](#) and 0.25 mL of [triethylamine](#) to each liter of the mixture.

Standard stock solution: 0.5 mg/mL of [USP Zolmitriptan RS](#) in *Diluent*

Standard solution: 0.025 mg/mL of [USP Zolmitriptan RS](#) from *Standard stock solution* and *Mobile phase*

System suitability stock solution: 0.005 mg/mL each of [USP Zolmitriptan Related Compound E RS](#) and [USP Zolmitriptan Related Compound G RS](#) in *Mobile phase*

System suitability solution: Dilute 1 mL of *System suitability stock solution* with 9 mL of *Standard solution*.

Sample stock solution: Nominally 0.5 mg/mL of zolmitriptan prepared as follows. Discharge the contents of NLT 10 units of Nasal Spray to a suitable container. Transfer an amount of the composite solution containing about 5 mg of zolmitriptan to a 10-mL volumetric flask. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.025 mg/mL of zolmitriptan from *Sample stock solution* in *Mobile phase*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 3-µm packing [L1](#)

Column temperature: 40°

Flow rate: 1.6 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of zolmitriptan

System suitability

Samples: *Standard solution* and *System suitability solution*

[NOTE—See [Table 1](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 4.0 between zolmitriptan and zolmitriptan related compound E, *System suitability solution*

Tailing factor: NMT 2.0 for zolmitriptan, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*



Analysis**Samples:** *Standard solution* and *Sample solution*Calculate the percentage of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) in the portion of Nasal Spray taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

 r_U = peak response from the *Sample solution* r_S = peak response from the *Standard solution* C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL) C_U = nominal concentration of zolmitriptan in the *Sample solution* (mg/mL)**Acceptance criteria:** 90.0%–110.0%**PERFORMANCE TESTS****• DELIVERED DOSE UNIFORMITY****Diluent, Mobile phase, Standard solution, and System suitability solution:** Prepare as directed in the Assay.**Sample solution:** Nominally 0.025 mg/mL of zolmitriptan prepared as follows. Discharge the contents of a single unit into a suitable volumetric flask. Dilute with *Mobile phase* to volume.

Repeat this procedure with 9 additional units.

Chromatographic system and System suitability: Proceed as directed in the Assay.**Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of zolmitriptan in each dose of Nasal Spray taken:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

 r_U = peak response from the *Sample solution* r_S = peak response from the *Standard solution* C_S = concentration of [USP Zolmitriptan RS](#) in the *Standard solution* (mg/mL) V = volume of the *Sample solution* L = label claim of zolmitriptan (mg/dose)**Acceptance criteria****Tier 1**

1. The mean of 10 units is within 85.0%–115.0% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$).
2. NMT 1 dosage unit outside of 80%–120% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$)
3. None outside of 75%–125% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$) for 10 units

If criterion 2 in *Tier 1* cannot be met, proceed to *Tier 2*.**Tier 2:** Test an additional 20 units. All 30 results (including the results from *Tier 1*) meet the following acceptance criteria.

1. NMT 3 of the 30 dosage units outside of 80%–120% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$)
2. None of the 30 dosage units are outside of 75%–125% of the labeled amount of zolmitriptan ($C_{16}H_{21}N_3O_2$).

IMPURITIES**• ORGANIC IMPURITIES****Diluent, Mobile phase, Standard solution, System suitability solution, and Sample stock solution:** Prepare as directed in the Assay.**Sensitivity solution:** 0.1 µg/mL of [USP Zolmitriptan RS](#) in *Mobile phase* from *Standard solution***Sample solution:** Nominally 0.1 mg/mL of zolmitriptan from *Sample stock solution* in *Diluent***Chromatographic system**(See [Chromatography \(621\)](#), [System Suitability](#).)**Mode:** LC**Detector:** UV 210 nm